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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,903	02/06/2004	J. P. Devlin		8342

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EXAMINER	
OLSON, ERIC	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/28/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/773,903	DEVLIN, J. P.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

This office action is a response to applicant's communication submitted November 29, 2006 wherein claims 1-6 are cancelled and new claims 7-13 are introduced. This application claims benefit of provisional application 60/445717, filed February 7, 2003.

Claims 7-13 are pending in this application.

Claims 7-13 as amended are examined on the merits herein.

Applicant's amendment, submitted November 29, 2006, with respect to the rejection of instant claims 1-6 under 35 USC 112, second paragraph as being indefinite for failing to clearly and distinctly identify formula III, and for failing to identify which statutory category the claimed invention belongs to, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are no longer pending.

Applicant's amendment, submitted November 29, 2006, with respect to the rejection of instant claims 4-6 under 35 USC 112, second paragraph as lacking antecedent basis in he parent claims, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are no longer pending.

Applicant's amendment, submitted November 29, 2006, with respect to the rejection of instant claims 1-6 under 35 USC 112, first paragraph as lacking written

description for therapeutic methods, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are no longer pending.

Applicant's amendment, submitted November 29, 2006, with respect to the rejection of instant claims 1-6 under 35 USC 112, first paragraph as lacking enablement for therapeutic methods, has been fully considered and found to be persuasive to remove the rejection as the rejected claims are no longer pending.

Applicant's amendment, submitted November 29, 2006, necessitates the following new grounds of rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7 is drawn to an improvement. It is unclear to which statutory category, (i.e. a process, machine, manufacture, or composition of matter as described in 35 USC 101) the claims are directed and which specific prior art process, machine, manufacture, or composition of matter is being improved by the claimed invention.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted November 29, 2006 with respect to amended claims 7-8 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for a collection or library of compounds for use in biological assays. The specification as originally filed merely describes how to make dihydrocelastrol compounds and suggests that they may have therapeutic utility.

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See Vas-Cath Inc v. Mahurkar, 19 USPQ 2d 1111 CAFC 1991, see also In re Winkhaus, 188 USPQ 129, CCPA 1975. Because Applicant's amendment necessitated this new ground of rejection, this rejection is made **FINAL**.

Claims 9-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Said claims appear to be drawn to therapeutic methods. However, Applicant's disclosure contains no descriptions of therapeutic methods for the treatment of inflammation, neurodegenerative diseases, or neoplastic diseases. No detains are given as to patient population, dosages or dosage forms, side effects, prognosis, or other factors involved in a therapeutic method. The mere description of a compound and listing of its potential utilities does not adequately convey that one has possession of all possible methods of using said compound. Therefore Applicant's disclosure fails to provide adequate written description of the claimed invention to demonstrate to a skilled artisan in a relevant field that Applicant has possession of the claimed invention.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is drawn to improvements in the treatment of neurodegenerative and neoplastic disease. The improvement comprises administering to a warm-blooded animal a compound of formula III, where formula III includes dihydrocelastrol, dihydropristimerin, their diacetates and related compounds.

The state of the prior art: No methods of treating any disease by administering compounds of formula III are known in the prior art. The parent compound on which these compounds are based, celastrol, is known to possess unacceptable cellular toxicity which prevents it from being a useful pharmaceutical compound. The compounds used in the claimed methods are known to induce heat-shock proteins, which may make them therapeutically useful in the treatment of diseases involving these proteins. However, not enough is known about this effect to provide the basis for a useful therapy. In fact, it would appear that the known cytoprotective effects of heat-

shock proteins may be counterproductive against neoplastic diseases. It is not generally taught in the art that the same treatment is effective for both neoplastic and neurodegenerative disorders, as the two categories of disease act in an opposite manner.

While the parent compound celastrol is a natural product component of a traditional Chinese remedy, the claimed invention is drawn to methods involving derivatives of this compound which are patentably distinct from celastrol. Therefore, the use of celastrol in traditional remedies for inflammatory conditions dose not enable one skilled in the art to practice a method of treating inflammatory conditions using the recited derivatives of celastrol having formula III.

It is speculated that the induction of heat-shock proteins by celastrol derivatives may provide the basis for treating Alzheimer's disease, prion diseases, and other conditions associated with accumulation of misfolded proteins. However, this theory has not been tested *in vivo*. Furthermore, this therapeutic approach is only expected to be useful for the treatment of diseases associated with protein misfolding. Neurodegenerative diseases such as amyotrophic lateral sclerosis, which involve as yet unknown mechanisms of neurodegeneration, are unlikely to be treated by a therapy specifically targeting protein folding. Neurodegenerative diseases are a diverse collection of maladies which have not been demonstrated to share one single cause which could be targeted by a single agent. Furthermore, no neurodegenerative diseases have ever been successfully treated by a therapy aimed at elevating heat-shock proteins.

With regard to neoplastic diseases, celastrol is also known to possess cellular toxicity which hinders its therapeutic use. (p. 2, last paragraph) While cellular toxicity is often a desirable property in a chemotherapy agent, it must be directed specifically toward cancerous cells in order to be an acceptable therapy. Otherwise it is merely a poison which is not useful for selectively killing neoplastic cells. In addition, Applicant admits in arguments submitted November 29, 2006, that the claimed compounds do not possess the toxic effects of celastrol. (p. 11, last paragraph under **6. The Invention**) Thus there is no reasonable expectation that the reduction in toxicity will not destroy the antineoplastic effects of these compounds.

Furthermore, the skilled artisan would view cancer as a group of maladies not treatable with one medicament or therapeutic regimen. No single chemotherapeutic drug is useful for the treatment of every case of cancer. Indeed, some types of cancer to not respond well to any known chemotherapeutic drugs. According to the Merck Manual of Diagnosis and Therapy (Reference of record in previous office action), Hepatocellular carcinomas and renal cell carcinomas are not generally improved by chemotherapy. Acute lymphoblastic leukemia, on the other hand, responds well to a number of drugs, including vincristine, anthracyclines, and aspariginases, while acute mylogenous leukemia, on the other hand, responds to fewer drugs and is usually treated with cytarabine in combination with daunorubicin or idarubicin. Breast cancer, on the other hand, is best treated with surgery and/or radiation, but the prognosis can be improved by the addition of adjuvant chemotherapy. As an illustration, Furbacher et al. (Reference included with PTO-892) disclose that a related celastrol derivative

possess toxicity against breast cancer cell line MCF-7 but not non-small-cell lung cancer line NCI-H460 and CNS glioma line SF-268. (p. 1295, right column, second paragraph)

Thus the existing state of the art does not enable one skilled in the art to practice a method of treating any cancers or neurodegenerative diseases by administering a compound of formula III.

The relative skill of those in the art: The relative skill in the art is high.

The predictability or unpredictability of the art: Neoplastic and neurodegenerative diseases are both broad categories encompassing numerous pathological conditions with diverse features. No one therapy is expected to be useful against all neoplastic diseases or all neurodegenerative diseases.

As mentioned above, no single treatment is effective for all cancers. Different cancers vary widely in their response to different chemotherapy regimens. According to the Oxford Textbook of Oncology, (Of record in the previous office action) "The important criteria for the tumor include its sensitivity to cytostatic drugs, its clinical stage and its mass, the presence of measurable lesions or biochemical markers, and, finally, growth characteristics," as well as, "*In vitro* sensitivity tests have been disappointing. They predict well for resistance but are of little use for sensitivity," (p. 451, right column, second paragraph) and, "For many types of cancer the potential benefit of chemotherapy has not been demonstrated in well-designed clinical trials."

Based on the known teachings of the prior art such as that stated above, one skilled in the art would recognize that it is highly unpredictable in regard to the treatment

in the instant case, including treating numerous and various tumors: gynecological tumors, ovarian carcinomas, testicle tumors, prostate carcinomas, skin cancer, kidney cancer, bladder tumors, esophagus carcinomas, stomach cancer, rectal carcinomas, pancreas carcinomas, thyroid cancer, adrenal tumors, various types of leukemia and lymphomas, Hodgkin's disease, tumor illnesses of the CAN, soft-tissue sarcomas, bone sarcomas, benign and malignant mesotheliomas, especially intestine cancer, liver cancer, breast cancer, bronchial and lung carcinomas, melanomas, acute and chronic leukemias and benign papillomatosis tumors, by performing the necessary experimentation to develop an optimized protocol for treating said cancers using compounds of formula III.

With regard to neurodegenerative diseases, there exists no agreed upon therapeutic target for treating all forms of neurodegeneration. While misfolded proteins have been suggested as a possible target for treatment of certain forms of neurodegeneration, this field has not been developed to the point where one skilled in the art could predict the effectiveness of such a therapeutic approach for all neurodegenerative diseases. Even for those diseases known to be associated with misfolded proteins, the claimed therapy will only be effective if the pharmacokinetic properties of the claimed compounds are such that they are delivered to the correct part of the body in the correct amounts for the correct duration, an assumption which has not been proven given the absence of any *in vivo* studies of the claimed compounds. This is an especially important consideration given that the compounds are supposed to act

by being converted into celastrol *in vivo*. (instant specification, p.3, last paragraph – p. 4, first paragraph)

Furthermore, administering a compound which has been shown to promote cell death under some circumstances may actually worsen the course of a neurodegenerative disease by promoting apoptosis. In the absence of *in vivo* data it is not possible to predict which effect will dominate under actual therapeutic conditions.

Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Additionally, the claims are interpreted to apply to new drugs for which comprehensive pharmacological data, such as optimal dosages and effectiveness against specific diseases, is not yet available.

The Breadth of the claims: The claims are drawn to the treatment of neurodegenerative and neoplastic diseases by administering a compound of formula III. No specific conditions are mentioned, so the claims cover all neurodegenerative or neoplastic diseases regardless of type or causes. For example, with regard to neoplastic diseases, the claimed invention is a method of treating any neoplastic condition without regard to which cell type it arises from, which tissue it occurs in, or which mutation triggered it.

The amount of direction or guidance presented: P. 1, under the heading, Background of the Invention, discloses that therapies targeting heat-shock proteins may be useful against inflammatory, neurodegenerative, or neoplastic diseases. P. 2, lines

7-10 disclose that celastrol has been reported to induce apoptosis in a human leukemia cell line. However, celastrol is not a compound of the present invention. Its derivative, dihydrocelastrol, is reported to possess less cellular toxicity (and thus less potential antineoplastic activity) than its parent compound. (p. 2, last paragraph, p. 4, first paragraph) No guidance is given as to how these findings may be adapted into an effective therapeutic method.

Dihydrocelastrol, dihydropristimerin, and their diacetates are shown to induce elevated levels of heat-shock protein HSP70. (Table, p. 5) However, no context is given as to the conditions of this experiment, such as whether it was performed *in vitro* or *in vivo*, what cell types were used, how long the cells were incubated with the test compounds, or whether the increased HSP70 led to relevant biological effects such as cytoprotection against apoptosis or reduced deposition of amyloid plaques.

The presence or absence of working examples: There are no working examples in Applicant's disclosure of any therapeutic use for compounds of formula III. In particular, there are no working examples of its use for the treatment of neurodegenerative or neoplastic disorders.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the treatment of neurodegenerative disease or cancer. See MPEP 2164.

The quantity of experimentation necessary: In order to use the disclosed information to practice the claimed invention for a wide range of diseases, a skilled practitioner of the art would develop a specific therapeutic regimen for each condition.

This would involve a process of optimizing and testing various regimens *in vivo* for each disease being treated. The skilled practitioner would start this process with no guidance from Applicant's disclosure as to the specific conditions expected to be treatable, the doses or dosage forms expected to be most effective, the frequency or duration of treatment, expected side effects, or any other details needed to devise an effective treatment regimen.

As the claimed compounds possess cellular toxicity, a study of their side effects would be undertaken before they could be reliably used for any therapeutic method. In addition to side effects stemming from cellular toxicity, side effects stemming from chronic up-regulation of heat-shock proteins would also be necessary, especially in the treatment of chronic neurodegenerative diseases, where a patient may be maintained on the therapy for the rest of their life in order to inhibit the progression of the disease. Determining the consequences of long-term therapy would require that the therapy be tested in a relatively long-lived animal model such as dogs, rather than in rodents which have too short of a lifespan to be useful for this purpose.

Furthermore, devising a therapeutic regimen for treating neurodegenerative diseases would involve the additional obstacle of finding suitable animal models. While certain conditions, such as prion diseases, are well studied in animals, no universally accepted animal model exists for Alzheimer's disease, for example. Thus experiments involving Alzheimer's disease would have to be repeated in several different model systems in order to reliably gauge the effectiveness of a particular therapy.

Still further, as neoplastic disorders are usually treated with combinations of drugs, the claimed methods would need to be modified to further take into account any positive or negative interactions with existing chemotherapy agents, necessitating yet more experimentation.

Therefore, given the absence of any guidance whatsoever from Applicant's disclosure beyond the mere suggestion that the disclosed compounds may be useful in therapeutic methods, one skilled in the art wishing to practice the claimed invention would be forced to undertake the development, from scratch, of many different therapeutic methods for many different and distinct diseases, many of which have never been treated successfully, using the same compounds as the active agent. This process would involve unpredictable experimentation which would constitute an undue experimental burden on the practitioner.

Genetech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the lack of guidance or working examples in Applicant's disclosure, Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Response to Argument: Applicant's argument, submitted November 29, 2006, with respect to the rejection of claims 1-6, now amended, on similar grounds as those described above, has been fully considered and not found persuasive to overcome the

rejection. Applicant asserts that new claims 7-12 fully comply with 35 USC 112, nut this assertion is not substantiated with arguments or facts from Applicant's disclosure as originally filed. Applicant recites (pp. 5-14) information concerning the claimed therapeutic activities of dihyrocelastrol and related compounds, but this information does not find support in the specification as originally filed at the time of invention. Therefore Applicant's argument is not found persuasive with regard to new claims 9-10.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Huang et al. (Reference included with PTO-892) Huang et al. discloses a collection of compounds having IL-1β inhibitory activity including several compounds of formula III. (p. 1884, table 1, compounds 1-6). These compounds are reasonably considered to be a collection or library according to instant claim 7. Thus the claimed invention is anticipated by Huang et al.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

Claims 7-8 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Takaishi et al. (Reference included with PTO-892) Takaishi et al. discloses a collection of compounds including several compounds of formula III. (p. 970, compounds **1 – 15**). Compound **15** in this collection is the species recited in instant claim 8. These compounds are reasonably considered to be a collection or library according to instant claims 7-8. These compounds are demonstrated to have anti-tumor activity against EBV-EA activated cells. (P. 972, right column, Table 3) Compounds **9**, **14**, and **15** are among those compounds which are especially active in this manner. Thus the claimed invention is anticipated by Takaishi et al.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-10 rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (Reference included with PTO-892) Huang et al. discloses a collection of compounds having IL-1β inhibitory activity including several compounds of formula III. (p. 1884, table 1, compounds 1-6). These compounds are reasonably considered to be

a collection or library according to instant claim 7. Compounds **1** and **2** differ in the presence of a free acid or methyl ester in the position corresponding to R_1 in the claimed formula III. Compound **5** is identical to the specific species of claims 8 and 10 except that R_1 is a methyl ester rather than a free acid. Similarly, compound **6** is a methyl ether of this species. In terms of inhibitory activity, the IC_{50} against IL-1β is lower in the free acid **1** than the methyl ester **2** and is lower in the acetylated species **5** than in the deacetylated species **4**. Compound **1** was used to treat streptococcal cell wall induced arthritis in rats in a method which is the same as that of instant claim 9. (p. 1885, bottom paragraph) Huang et al. does not explicitly disclose a library or method involving the specific compound of claim 8 or a therapeutic method using the species of claims 8 and 10.

It would have been obvious to one of ordinary skill in the art at the time of the invention to produce a collection or library containing the compound of claim 8, and to use the compound in a method of treating inflammatory conditions such as inflammatory arthritis according to claims 9 and 10. One of ordinary skill in the art would have been motivated to use this compound because it bears a close resemblance to species disclosed by Huang et al. and because removal of the methyl group from compound **5** is reasonably expected to yield a compound with at least as strong inhibitory activity against IL-1β, in view of the relation between compounds **1** and **2**. One of ordinary skill in the art would have been motivated to use the compound to treat inflammatory arthritis because it has a structure and expected IL-1β inhibitory activity similar to that of compound **1**, which is disclosed to be useful in such a method. One of ordinary skill in

the art would reasonably have expected success because compounds **1-6** have close structural similarity to each other and to this compound.

Thus the invention taken as a whole is *prima facie* obvious.

Because Applicant's amendment necessitated the above new grounds of rejection, this rejection is made **FINAL.**

Summary

No claims are allowed in this application. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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